NCI-FREDERICK
INSTITUTIONAL BIOSAFETY COMMITTEE

Minutes – Meeting June 15, 2004
NCI-Frederick

The NCI-Frederick Institutional Biosafety Committee was convened at 12:00 p.m. in the Building 549 Executive Boardroom with the following members in attendance:

Dr. Randall Morin, Chair
Mr. Joseph Kozlovac, Secretary
Dr. Bruce Crise
Dr. Melinda Hollingshead
Dr. Steve Hughes
Mr. Lucien Winegar, Esq
Dr. Henry Hearn
Ms. Carol Ingraham Tobias
Dr. Stephen Creekmore
Dr. Jeanne Herring
Dr. Donald Court

Members not in attendance: Dr. Michael Baseler, Dr. David Garfinkel and Ms. Cheryl Parrott (Ex Officio)

Others in attendance: Ms. Cara Lamberson, Mr. Tom Danver, Ms. Kathleen Nalewaik, Ms. Phyllis Taliaferro, Dr. Denise Ekstrom, Dr. Ray Harris and Dr. Steve Giardina

INTRODUCTION

Dr. Morin called the meeting to order. Ms. Tobias introduced Kathleen Nalewaik, CRNP, COHNR the Occupational Health Services (OHS) Clinical Manager who presented to the committee an overview of medical surveillance programs as it relates to biological agents as well as a review of post-exposure treatment and follow up provided by OHS.

REVIEW OF PROTOCOLS

Mr. Kozlovac introduced a registration document entitled, *Adenovirus Δ24-RGD For Glioblastoma and Ovarian Cancer*, submitted by Dr. Ray Harris and Dr. Denise Ekstrom. Mr. Kozlovac informed the committee that this work is an adjunct to registration P180303JLA01 which was approved on March 18.2003. This registration will cover the 2nd phase of this project, which involves an increase in process scale, staff involved and additional laboratory space. The PIs wish to culture and purify up to 10L of Adenovirus Δ24-RGD within recently

acquired BSL-2 laboratory space. Mr. Kozlovac informed the committee that a few members of the IBC and himself had visited the laboratory on June 3, 2004 and that there was some concern with the proposed laboratory in conducting work with a significant volume of fairly high titer material. Mr. Kozlovac asked Dr. Ekstrom to review the BDP's proposal and how they proposed to address some of the procedural and facility issues that were raised on the initial visit. Dr. Ekstrom reviewed the process, which involves producing virus in HEK A549 cells, grown on Cytodex-3 microcarriers, inside a Wave Bioreactor. The Wave Bioreactor is essentially a very strong plastic bag that rests on a rocker platform. When sufficient viral titer and volume have been attained the supernatant will be harvested into centrifuge bottles, centrifuged at 6,000 rpm, the cell pellet would then be re-suspended in lysis buffer which disrupts the remaining cells and releases the virus which is then further separated and clarified to provide the final live virus product. Dr. Ekstrom informed the committee that based on the June 3, 2004, suggestions of the IBC members that toured the proposed lab that they intended to perform a mock run using water. Dr. Hughes asked how they intended to get the fluid out of the bag and into the centrifuge tubes. Dr. Ekstrom described a process of removing the Wave Bag from the ventilated cabinet onto a cart which shall be moved near the class II biological safety cabinet and the fluid would be pumped into the centrifuge tubes located within the BSC. Dr. Hollingshead recommended placing the bag in a box or container that could be sealed and withstand dropping. Dr. Ekstrom informed the committee that they had planned to use a "Rubbermaid" container on the cart. Dr. Creekmore asked if would be possible to not move the bag out of the ventilated cabinet but rather using a portable "sterile hood" to make the tubing connections and run tubing from the bag in the ventilated cabinet to the BSC where the centrifuge tubes could be filled. Mr. Kozlovac stated that he was concerned about having several feet of flex tubing between the two ventilated engineering controls. Mr. Kozlovac suggested that if such a system were considered than the tubing would need to be housed within a secondary piping/tubing (i.e stainless steel or PVC). Dr. Hearn asked that since the existing facility was not ideal for the work that the BDP wished to conduct are there plans to construct more adequate facilities in the future or was there other more appropriate facilities available. Dr. Creekmore responded that this was newly acquired space for the BDP program and that financing for the construction of new facilities essentially required an act of Congess. Mr. Kozlovac suggested since we had other protocols to review that the committee take time to review the packet, which they received at the meeting and provide comments to his office as appropriate. Mr. Kozlovac further suggested that Dr. Ekstrom provide advance notice of when the practice run was going to be conducted so that those committee members that wished to observe and comment on the planned process could do so.

TABLED – Pending scheduled mock run and further IBC review and comments.

Dr. Creekmore introduced a new pathogen registration submitted by Dr. James Phang entitled, *Metabolic regulation of apoptosis*. This protocol involves the use of human unfixed tissues obtained from the Cooperative Human Tissue Network in procedures to include RNA preparations for RT-PCR, Northern blots and protein preparations for western immunoblots. Dr. Creekmore thought that the answer provided in Part C question #5 of the registration was not appropriate. The question, "Has material been prescreened for pathogens?" was answered "Don't Know" and Dr. Creekmore indicated that he would like the PI to provide more information. Ms. Tobias noted that in Part A, #2, which lists personnel involved with this project who may be at risk of potential exposure and provides a space for them to initial to indicate that they have been informed of potential hazards, safe work practices, etc, that all the initials appeared to be in the same handwriting and was concerned that perhaps the involved employees were not appropriately notified regarding the exposure risks. Drs. Hughes, Crise and Hollingshead suggested that this registration be tabled until Mr. Kozlovac can clear up the questions regarding the form with Dr. Phang to the satisfaction of the IBC lead reviewer (Dr. Creekmore).

TABLED – Mr. Kozlovac will contact PI to resolve issues/questions

Dr. Melinda Hollingshead introduced a new rDNA registration submitted by Dr. Peter Nissley entitled, *Tumorigenesis of mouse embryo fibroblasts transfected with insulin-like growth factor I receptor constructs*. Dr. Hollingshead indicated that the animal work only will be conducted at NCI-Frederick and that the registration, which utilizes a plasmid-based system, was fairly straightforward. The only issue of concern that question #15 on the form, *Have all personnel associated with this protocol (including animal caretakers) been instructed and trained in the practices and techniques required to ensure safety and the procedures for dealing with accidents,* was not answered and the roster of involved staff was not provided. Mr. Kozlovac indicated that the animal facility manager and the PI had resolved the issue. Ms. Lamberson provided the roster to Dr. Hollingshead that was sent by the animal facility manager to EHS after Ms. Lamberson had distributed the registration packets to the members.

APPROVED

Dr. Bruce Crise introduced an amendment to P230902JLA01, P150703RHA01, P190701JLA01 and P180303JLA01 submitted by Dr. Gopalan Soman through the Principle Investigators, Dr. Raymond Harris and Dr. Jinhua Lu, of the listed registrations. The amendment wishes to add new labs and staff to the listed registrations for the purpose of assay development related to these viral vector projects. Dr. Crise was concerned regarding some of the generality of some of the statements (i.e. operations that involve the manipulation will be contained within BSCs and if possible assays will be conducted within BSCs.). Dr. Crise would like for them to put in a statement to the effect that "No work with infectious or potentially infectious materials will be conducted on the open bench". Dr.

Hughes expressed it might be useful for the researcher to state what types of activities that they would not perform without prior approval from the committee. Dr. Hearn asked Mr. Kozlovac if he had seen these labs as of yet. Mr. Kozlovac stated that he has visited the lab and had made a number of recommendations including the addition of a door between the two connecting laboratories. Mr. Kozlovac indicated that the laboratories met BSL-2 requirements and that he thought the FME designed Plexiglass ventilated enclosure was an improvement over having the HPLC on the open bench.

CONDITIONALLY APPROVED – BDP to provide requested statement and to remove general statements from the original submission.

The following information was discussed outside of the regular monthly meeting of the IBC since the IBC had to adjourn prior to discussing all agenda items. This information is incorporated into these minutes as a mechanism for maintaining a record of items listed on the agenda discussed by IBC members and EHS staff outside of the regular meeting.

Renewal of registration P201101SHA01
Drs. Hollingshead and Herring concluded that the pathogen renewal registration submitted by Dr. Perez Hussain entitled, *Effect of C. parvum on tumorigenicity*, involving heat inactivated *C. parvum* did not need full committee review.

APPROVED

Renewal rDNA registration 04-04
Drs. Hollingshead and Herring concluded that the rDNA renewal registration submitted by Dr. Dimiter Dimitrov entitled, *Development of anti-viral vaccines, human antibodies and cancer antigens by using recombinant proteins*, involving the expression and use of various viral membrane proteins or cancer specific antigens did not need full committee review.

APPROVED

Renewal rDNA registration 04-07
Drs. Hollingshead and Herring concluded that the rDNA renewal registration submitted by Dr. John Ortaldo entitled, Use of rDNA in in-vitro and in-vivo studies, involving mammalian (murine & human) cDNA genes coding for cytokine or lymphocyte proteins to cloned into a plasmid for introduction into mice for expression of protein of interest, did not require full committee review. EHS has yet to receive project staff signatures and approval will be pending until received.

CONDITIONALLY APPROVED – pending receipt of staff signatures by EHS

OLD BUSINESS
The rDNA registration submitted by Dr. Shyam Sharan entitled, *Functional Analysis of Breast Cancer Susceptibility Genes,* discussed at the May meeting of the IBC and tabled pending input from the IBC lead reviewers Drs. Hollingshead and Herring was approved on 6/4/2004.

Meeting Adjourned: 2:00 p.m.

Respectfully submitted,

Joseph P. Kozlovac, M.S., CBSP, RBP
Executive Secretary, NCI-Frederick
Institutional Biosafety Committee

Approved: _____ Randall S. Morin, Dr. P.H.
Chairman, NCI-Frederick IBC

xc: Each Committee Member
Dr. Wiltrout
Dr. Reynolds
Mr. Eaton
Dr. Arthur
Mr. Bufter